

Claims

1. (Previously presented) A humanized anti-TAG-72 CC49 antibody comprising:  
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,  
and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2,  
and a H-CDR3,  
wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 comprise murine  
monoclonal CC49 antibody Complementarity Determining Regions (CDRs) and at least one of  
L-CDR1 and L-CDR2 are a human monoclonal LEN antibody L-CDR1 and L-CDR2,  
wherein the humanized CC49 antibody retains binding affinity for TAG-  
72 and has reduced immunogenicity, as compared to a parental humanized CC49 antibody.
2. (Previously presented) The humanized antibody of claim 1, wherein L-CDR1 is  
the human monoclonal LEN antibody L-CDR1.
3. (Canceled)
- ~~3~~ ~~4.~~ (Previously presented) The humanized antibody of claim 1, wherein L-CDR2 is  
the human monoclonal LEN antibody L-CDR2.
5. (Canceled)
- ~~4~~ ~~6.~~ (Previously presented) The humanized antibody of claim 1, wherein both L-  
CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.
- 7-9. (Canceled)
- ~~5~~ ~~10.~~ (Previously presented) The humanized antibody of claim 1, wherein the parental  
humanized CC49 antibody comprises three L-CDRS and three H-CDRs of the murine  
monoclonal CC49 antibody, a variable light chain framework of a human monoclonal LEN  
antibody, and a variable heavy chain framework of a human monoclonal 21/28'CL antibody.

6 11. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:  
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,  
and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2,  
and a H-CDR3,

wherein at least L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a  
murine CC49 monoclonal antibody ~~L-CDR3, H-CDR1, H-CDR2 and H-CDR3~~, and wherein L-  
CDR1 and L-CDR2 are ~~murine CC49 antibody or of a human monoclonal LEN antibody~~ L-  
CDR1 and L-CDR2 respectively, and wherein at least one amino acid at position 60, 61, 62, or  
64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding position in  
the human monoclonal 21/28'CL antibody,

wherein the humanized CC49 antibody retains binding affinity for TAG-  
72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

7 12. (Previously presented) The humanized antibody of claim 11, wherein an  
asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

8 13. (Previously presented) The humanized antibody of claim 11, wherein a threonine  
at position 97 of the murine CC49 L-CDR3 is replaced with a serine.

14. (Canceled)

9 15. (Previously presented) The humanized antibody of claim 11, wherein L-CDR1 is  
a human monoclonal LEN antibody L-CDR1.

16. (Canceled)

10 17. (Previously presented) The humanized antibody of claim 11, wherein L-CDR2 is  
a human monoclonal LEN antibody L-CDR2.

18. (Canceled)

19. (Previously presented) The humanized antibody of claim 11, wherein both L-CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.

20. (Canceled)

21. (Previously presented) The humanized antibody of claim 11, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

22. (Previously presented) The humanized antibody of claim 11, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

23. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:  
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,  
and a L-CDR3; and a heavy chain Complementarity Determining Region (H-CDR)1, a H-CDR2,  
and a H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49  
monoclonal antibody L-CDR3, H-CDR1, H-CDR2 and H-CDR3, and wherein L-CDR1 and L-  
CDR2 are murine CC49 antibody or of a human monoclonal LEN antibody L-CDR1 and L-  
CDR2 respectively, and wherein a threonine at position 97 in the murine CC49 L-CDR3 is  
replaced with a serine,

wherein the humanized CC49 antibody retains binding affinity for TAG-  
72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

24. (Previously presented) The humanized antibody of claim 23, wherein at least one amino acid of positions 60, 61, 62, or 64 in the murine CC49 H-CDR2 is replaced with an amino acid at a corresponding position in the human monoclonal 21/28'CL antibody.

25. (Canceled)

26. (Previously presented) The humanized antibody of claim 23, wherein L-CDR1 is a human monoclonal LEN antibody L-CDR1.

27. (Canceled) *14*

*17* 28. (Previously presented) The humanized antibody of claim 23, wherein L-CDR2 is a human monoclonal LEN antibody L-CDR2.

29. (Canceled) *14*

*18* 30. (Previously presented) The humanized antibody of claim 23, wherein both L-CDR1 and L-CDR2 are human monoclonal LEN antibody L-CDR1 and L-CDR2, respectively.

31-33. (Canceled)

*19* 34. (Currently amended) A humanized anti-TAG-72 CC49 antibody comprising:  
a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,  
and a L-CDR3; and a heavy chain Complementarity Determining (H-CDR)1, a H-CDR2, and a  
H-CDR3,

wherein L-CDR1, L-CDR2, L-CDR3, H-CDR1, H-CDR2 and H-CDR3  
are of a murine CC49 antibody and L-CDR1 and L-CDR2 are of a human monoclonal LEN  
antibody L-CDR1 and L-CDR2 respectively, and

wherein (1) a threonine is at position 94 in the L-CDR3, or (2) a serine is at position 97 in the L-CDR3, or (3) a threonine is at position 94 and a serine is at position 97 in the L-CDR3,

wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

*20* 35. (Currently amended) The humanized antibody of claim 34, A humanized anti-  
TAG-72 CC49 antibody comprising:

a light chain Complementarity Determining Region (L-CDR)1, a L-CDR2,  
and a L-CDR3; and a heavy chain Complementarity Determining (H-CDR)1, a H-CDR2, and a  
H-CDR3,

wherein L-CDR3, H-CDR1, H-CDR2 and H-CDR3 are of a murine CC49 antibody and L-CDR1 and L-CDR2 are of a human monoclonal LEN antibody L-CDR1 and L-CDR2 respectively, and

wherein the a threonine is at position 94 in the L-CDR3,  
wherein the humanized CC49 antibody retains binding affinity for TAG-72 and has reduced immunogenicity, when compared to a parental humanized CC49 antibody.

36-37. (Canceled)

21 38. (Previously presented) A pharmaceutical composition, comprising a therapeutically effective amount of the humanized antibody of claim 1 in a pharmaceutically acceptable carrier.

39. (Canceled)

22 40. (Previously presented) A composition comprising a functional fragment of the humanized antibody of claim 1, wherein the functional fragment specifically binds TAG-72.

23 41. (Previously presented) The composition of claim 40, wherein the fragment comprises an Fv, an Fab, or an F(ab')<sub>2</sub>.

42-47. (Canceled)

24 48. (Previously presented) The humanized antibody of claim 2, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

25 49. (Previously presented) The humanized antibody of claim 4, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

26 50. (Previously presented) The humanized antibody of claim 6, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

27 51. (Previously presented) The humanized antibody of claim 11, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

28 52. (Previously presented) The humanized antibody of claim 11, wherein the amino acid at the corresponding position in the human monoclonal 21/28'CL antibody comprises an amino acid corresponding to position 12, 13, 14, or 16 of the amino acid sequence as set forth in SEQ ID NO: 11.

29 53. (Previously presented) The humanized antibody of claim 11, wherein the parental humanized CC49 antibody comprises three L-CDRs and three H-CDRs from the murine monoclonal CC49 antibody, a variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

30 54. (Previously presented) The humanized antibody of claim 15, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

31 55. (Previously presented) The humanized antibody of claim 17, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

32 56. (Previously presented) The humanized antibody of claim 18, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

33 57. (Previously presented) The humanized antibody of claim 23, wherein the parental humanized CC49 antibody comprises three L-CDRs and three H-CDRs from the murine monoclonal CC49 antibody, a variable light chain framework from a human monoclonal LEN antibody, and a variable heavy chain framework from a human monoclonal 21/28'CL antibody.

24 58. (Currently amended) The humanized antibody of claim 24, wherein the amino acid at position 60 is a serine, the amino acid at position 61 is a glutamine, the amino acid at position 62 is a lysine, or the amino acid at position 64 is a glutamine the corresponding position in the human monoclonal 21/28'CL antibody comprises amino acid 12, 13, 14, or 16, respectively, of an amino acid sequence as set forth in SEQ ID NO: 11.

25 59. (Previously presented) The humanized antibody of claim 24, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine.

26 60. (Previously presented) The humanized antibody of claim 24, wherein a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine.

27 61. (Previously presented) The humanized antibody of claim 24, wherein an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine.

28 62. (Previously presented) The humanized antibody of claim 24, wherein a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

29 63. (Previously presented) The humanized antibody of claim 26, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7.

30 64. (Previously presented) The humanized antibody of claim 28, wherein the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

31 65. (Previously presented) The humanized antibody of claim 30, wherein the human L-CDR1 comprises an amino acid sequence as set forth in SEQ ID NO: 7 and the human L-CDR2 comprises an amino acid sequence as set forth in SEQ ID NO: 8.

32 66. (Previously presented) The humanized antibody of claim 34, wherein the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

43. 67. (Previously presented) The humanized antibody of claim 34, wherein the threonine is at position 94 in the L-CDR3 from the murine CC49 antibody and the serine is at position 97 in the L-CDR3 from the murine CC49 antibody.

44. 68. (Previously presented) The humanized antibody of claim 61, wherein an asparagine at position 60 in the murine CC49 H-CDR2 is replaced with a serine, a glutamic acid at position 61 in the murine CC49 H-CDR2 is replaced with a glutamine, an arginine at position 62 in the murine CC49 H-CDR2 is replaced with a lysine, and a lysine at position 64 in the murine CC49 H-CDR2 is replaced with a glutamine.

45. 69. (Previously presented) A kit comprising a container comprising the humanized antibody of claim 1 and instructions for using the humanized antibody to treat or detect a cancer cell expressing TAG-72.

46. 70. (new) The humanized antibody of claim 68, wherein a threonine at position 97 of the murine CC49 L-CDR3 is replaced with a serine.

47. 71. (new) The humanized antibody of claim 70, wherein the humanized antibody is radiolabeled.